Sorafenib (Nexavar®)

Criteria for Use in Hepatocellular Carcinoma (HCC)

November 2010

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient. Individual cases that are outside the recommendations should be adjudicated at the local facility according to the policy and procedures of its P&T Committee and Pharmacy Services.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive sorafenib.*

- 1. Patient is a candidate for transplantation
- 2. Liver dysfunction categorized as Child-Pugh class C [see Issues for Consideration]
- 3. Renal dysfunction requiring hemodialysis [see Issues for Consideration]
- 4. Patient declines transfer of HCC care (including treatment decisions and follow-up) to VA hepatology or oncology provider
- 5. Patient is unable to comprehend and/or comply with dosing instructions
- 6. Patient is non-compliant with appointments for blood work

Inclusion Criteria *All of the following must be met in order to meet criteria.*

- 1. Documented diagnosis of advanced HCC – defined as unresectable or metastatic
- 2. ECOG performance status 0, 1 or 2
- 3. Liver dysfunction categorized as Child-Pugh class A or B* [*see Issues for Consideration]
- 4. Adequate hematologic function – defined as hemoglobin $\geq$ 8.5 g/dL, platelet count $\geq$ 60 x 10^9 /L
- For female patients or male patients (with female partners of childbearing potential):
  - Sorafenib may cause birth defects or death of an unborn baby.
  - A pregnancy test should be performed on pre-menopausal female patients prior to beginning sorafenib.
  - Male patients should inform sexual female partners (of child-bearing potential) that sorafenib may cause birth defects or death of an unborn baby.
  - Male and female patients should be provided contraceptive counseling on the potential risk vs. benefit of taking sorafenib if they or their partner were to become pregnant. Sexually active patients (involving a female of child-bearing potential) should use effective birth control methods during treatment and for at least 2 weeks after stopping sorafenib.
  - Female patients should be advised against breast-feeding while being treated with sorafenib

Dosage and Administration

- Sorafenib 400 mg (2 x 200 mg tablets) twice daily without food, at least 1 hr before or 2 hrs after eating [see Issues for Consideration]
- Dose interruption and/or dose reduction may be necessary to manage adverse events. Refer to Package Insert for specific instructions
- Use of concomitant strong CYP3A4 inducers (e.g. St. John's Wort, dexamethasone, phenytoin, carbamazepine, rifampin) may reduce plasma concentrations of sorafenib and should be avoided. If a strong inducer must be given with sorafenib, consider increasing the dose of sorafenib and monitor for toxicity
- Radiologic imaging should be performed every 6 – 12 weeks with plan to discontinue sorafenib if evidence of progressive disease is noted.

Issues for Consideration

- Sorafenib is a non-formulary item
- Sorafenib trials have excluded patients who have received prior systemic therapy for HCC, therefore the safety and efficacy of sorafenib in patients who have received prior systemic therapy is unknown. Use of sorafenib, in this setting, should be evaluated on a case-by-case basis.
- Child-Pugh class B: the majority of those studied in the clinical trial setting were classified as Child-Pugh class A; a small portion of the study population were Child-Pugh class B, therefore caution should be used when extrapolating data to this population
- Child-Pugh class C: sorafenib has not been studied in this population
- Drug-drug interactions: concomitant CYP3A4 inducers should be avoided. [Refer to Dosage and Administration]
- Dosing: No dosage adjustment is necessary based on mild, moderate or severe renal insufficiency not undergoing dialysis. Sorafenib has not been studied in patients undergoing dialysis. A phase I pharmacokinetic study suggests a lower initial dose in those with severe hepatic or renal dysfunction. Use caution and close monitoring in these populations.
- Pregnancy category D: For female patients or male patients (with female partners of childbearing potential): Sorafenib may cause birth defects or death of an unborn baby. A pregnancy test should be performed on pre-menopausal female patients prior to beginning sorafenib. Male patients should inform sexual female partners (of child-bearing potential) that sorafenib may cause birth defects or death of an unborn baby. Male and female patients should be provided contraceptive counseling on the potential risk vs. benefit of taking sorafenib if they or their partner were to become pregnant. Sexually active patients (involving a female of child-bearing potential) should use effective birth control methods during treatment and for at least 2 weeks after stopping sorafenib. Female patients should be advised against breast-feeding while being treated with sorafenib
- Hand-foot skin reaction is a common adverse event, usually occurring within the first 6 weeks of therapy. Educate patients and inform them to report redness, pain, swelling or blisters on the palms of the hands or soles of the feet. Dose-modification may be necessary.
- Blood pressure monitoring: Treatment-related hypertension can occur early in the course of therapy, therefore regular monitoring is recommended.
- Cardiac ischemia/infarction is considered to be an uncommon adverse event, although the incidence of ischemia/infarction was higher in the sorafenib-treated groups compared to placebo. Providers should discuss the possibility of cardiac ischemia/infarction with patients and educate them to report any episodes of chest pain or other related symptoms.
- Bleeding risk may increase due to sorafenib therapy. INR elevations in patients taking warfarin have been reported. Educate patients and inform them to promptly report any episodes of bleeding.
- Gastrointestinal perforation has been reported with sorafenib in < 1% of patients. Educate patients and inform them to report abdominal pain, which may or may not be accompanied by nausea, vomiting or high fever.
- Wound healing complications may occur if surgery is performed while a patient is taking sorafenib. If a major surgical procedure is needed, temporary interruption of sorafenib is recommended. Sorafenib may be restarted after adequate wound healing.